



International Journal of
Cancer Research

ISSN 1811-9727



Academic
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Molecular Marker Could Help Spot Pancreatic Cancer Early

Researchers at the University of North Carolina at Chapel Hill School of Medicine have identified a molecular marker of pancreatic cancer that may help spot the disease at its earliest stages, when it can be treated more successfully with surgery.

In a finding published April 26, 2010, in the online journal PLoS ONE, the researchers showed that a specific form of a protein called palladin is produced in large amounts in the "tumor nest," the cells that surround a pancreatic tumor.

By measuring the levels of this form of palladin in patient samples, doctors could have an improved way to screen for the deadly cancer, possibly catching it earlier than ever before, said senior study author Carol Otey, Ph.D., Associate Professor of Cell and Molecular Physiology at UNC.

Otey is a member of the NC Translational and Clinical Sciences Institute (NC TRaCS), part of a collaborative effort of a national network of medical research institutions affiliated with the NIH Clinical and Translational Science Awards (CTSAs).

"The problem with pancreas cancer is it is almost never caught at an early stage," said Otey. "By the time a person develops suspicious symptoms, the disease has typically progressed too far. But if you can diagnose it early, it can be treated very effectively with surgery."

Palladin, a protein which Otey discovered a decade ago, plays an important role in cell motility, adhesion and structure. More recently, Otey and her collaborator Teri Brentnall at the University of Washington showed that palladin was mutated in an inherited form of pancreas cancer and was also produced in large amounts -- "upregulated" -- in a number of sporadic pancreas tumors.

Otey and her colleagues decided to see if this upregulation of palladin could provide a useful diagnostic tool for identifying the disease at earlier stages. They knew that the single palladin gene message can actually be cut and

pasted together in a manner that produces at least seven different palladin protein products. Turns out only a couple of these forms of palladin -- called isoforms -- appear in pancreatic tissue.

The researchers found that the longer of these two isoforms was upregulated in the cells surrounding the tumor -- called tumor-associated fibroblasts -- when compared to normal pancreas. Their findings were consistent, regardless of whether they were looking in cultured cell lines, patient samples, or tumors from a mouse model.

Otey thinks that the upregulation of this form of palladin in tumor-associated fibroblasts could help them become contractile and stiff -- more like muscle than connective tissue -- in order to generate channels through neighboring tissue so the cancer can metastasize and spread.

"The interactions between these tumor-associated fibroblasts and tumor cells are really important and are probably what is causing pancreas cancer to be so deadly, invasive and resistant to current therapies," said Otey.

And that is why raising public awareness and enhancing our abilities to diagnose the disease early is so critical, says Hong Jin Kim, Associate Professor of Surgery at UNC, who along with Otey is senior author of the study.

"It appears that the upregulation of palladin in the tumor-associated fibroblasts is an early event in the neoplastic process," said Kim. "We may be able to take advantage of these findings, since pathologic confirmation of pancreatic adenocarcinoma in the preoperative setting is often

difficult, requiring an invasive procedure directed by endoscopic ultrasound. If we can enhance the diagnostic efficiency of these studies by staining for palladin, it would be clinically helpful for interventional gastroenterologists and pathologists.”

The UNC research was funded in part by the Elsa U. Pardee Foundation and the National Institutes of Health. Study co-authors from UNC include first author Silvia M. Goicoechea, Brian Bednarski, Christianna Stack, David W. Cowan, Keith Volmar, Jen-Jen Yeh, and Leigh Thorne.

Other study co-authors are Sunil Hingorani of the Fred Hutchinson Cancer Research Center, Seattle, WA; Edna Cukierman, Fox Chase Cancer Center, Philadelphia, PA; Anil K. Rustgi, University of Pennsylvania; Teresa Brentnall, University of Washington; Rosa F. Hwang, University of Texas M.D. Anderson Cancer Center, Houston, TX; Christopher A.G. McCulloch, University of Toronto, Canada; David J. Bentram, Northwestern Medical Faculty Foundation, Chicago, IL; and Steven Hochwald, University of Florida College of Medicine, Gainesville, FL.

Source: PLoS ONE, 2010; DOI: 10.1371/journal.Pone.0010347